REMARKS

Rejection of Claims 3, 6, and 6 Under 35 USC §112, Second Paragraph:

This rejection is respectfully traversed because words of approximation, such as "about," have been deemed to be clear and unambiguous in a great many cases and, as used in the present claims, the word "about" is used in a clear and unambiguous fashion. See MPEP §2173.05(b).

With respect to the subscripts "n" and "m" as recited in Claim 3, please note that the base claim (Claim 1) positively requires that $n + m = 1$. Therefore, any variation in the value of "n" or "m" must be compensated by an inverse variation in the other so that the equation $n + m = 1$ is satisfied. Thus, if the word "about" permits the values to vary by 10% or 50%, this does not render the claim unclear because $n + m$ must equal 1 accordingly to the positive requirements of Claim 1. By way of a simple example, if the word "about" allows the upper and lower values of "n" to vary by +/- 10%, that yields and expanded range of 0.27 to 0.77 for the value of "n" (*i.e.*, the lower limit goes down 10% and the upper limit goes up 10%) and a contracted range of 0.33 to 0.63 (*i.e.*, the lower limit goes up 10% and the upper limit goes down 10%). In either instance, the requirement that $n + m = 1$ must still be met. So for the expanded range for "n" (0.27 to 0.77), the subscript "m" **must** necessarily be 0.73 to 0.23 to satisfy the requirement that $n + m = 1$. Likewise, for the contracted range for "n" (0.33 to 0.63), the subscript "m" **must** necessarily be 0.67 to 0.37 to meet the requirements of Claim 1.

The same situation holds true with respect to the subscripts x, y, and z in Claim 6. Claim 6 ultimately depends from Claim 1, and Claim 1 positively requires that $x + y + z = 1$. Therefore any variation in any of the subscripts x, y, or z permitted by the word "about" must necessarily be compensated by a corresponding inverse change in one or two of the other subscripts so that the positive requirement of Claim 1 that $x + y + z = 1$ is met.

With respect to Claim 7, Applicants note that the values prefaced by the word "about" are values that are not amenable to utterly exact and precise quantification (weight average molecular weight [Mw] and percent vinyl butyral groups). Using the word "about" as applied to these types of values is a long-practiced and accepted claiming strategy under 35 USC §112.

Applicants therefore submit that this rejection is untenable. Withdrawal of the rejection is respectfully requested.

Rejection of Claims 1-9 under 35 USC §103(a) Over Ding (U.S. Patent No. 7,294,329) in View of Hsu et al. (U.S. Patent No. 6,340,465) and the Kollidon VA 64 Technical Information ("Kollidon reference"):

This rejection is respectfully traversed because the combination of references does not teach or suggest the three-part combination required by Claim 1. Specifically, Claim 1 requires a "bioactive material," a "first compound," and a "second compound." The first compound is a ternary, random copolymer comprised of a vinyl acetal monomers, vinyl alcohol monomers, and vinyl acetate monomers. The second compound is a binary copolymer comprised of vinyl pyrrolidone monomers and vinyl acetate monomers. The combination of Ding, Hsu et al, and the Kollidon reference does not describe or suggest the three-part composition recited in Claim 1 because the references do not provide any motivation for combining a poly(vinyl butyral-co-vinyl alcohol-co-vinyl acetate) copolymer ("PVB," *i.e.*, the first compound) with a poly(vinyl pyrrolidone-co-vinyl acetate) copolymer ("PVP/PVA," *i.e.*, the second compound).

Applicants further note that this rejection is improper because combining Ding with Hsu et al. destroys the intended utility (drug elution) of the Ding device. Thus, the Office has not established a prima facie case of obviousness.

Lastly, because the references themselves do not provide any motivation to make the combination, Applicants further submit that this rejection is improper because the Office is using Applicants' own specification to provide the motivation or suggestion that is lacking in the cited references.

The Ding patent describes using a PVB copolymer as a coating for an implantable medical device, including a stent. See Ding at column 2, lines 40-65. The Ding patent, however, is **completely silent** with respect to using any type of vinyl pyrrolidone-containing polymer or copolymer in combination with the PVB shown in Formula I of Ding (at the bottom of column 2). For example, Ding notes that "other examples" of polymers that can be used in his invention are poly(vinyl formal), poly(vinyl formal-co-vinyl alcohol-co-vinyl acetate, and mixed poly(acetal)-based polymers. These various copolymers can be used singly or blended. See Ding at column 2, lines 55-67. Nevertheless, Ding et al. neither describes, nor suggests using any type of vinyl pyrrolidone-containing polymer or copolymer.

The Office thus cites to the Hsu et al. patent for its description of a PVP/PVA copolymer. However, there is no motivation to combine Hsu et al. with Ding et al. because the manner in which Hsu et al. use a PVP/PVA copolymer has nothing whatsoever to do with drug eluting devices. In fact, combining the PVP/PVA copolymer described by Hsu et al. with the PVB described by Ding destroys the intended utility of the Hsu et al. device. Applicants therefore submit that this rejection is improper.

Specifically, the abstract of the Hsu et al. patent states that biocompatible surfaces on medical devices are formed by creating a stable, lubricious, cross-linked base layer. Note, however, that this cross-linked base layer functions as an entrapping site for "biocompatible agents," which are then "stably" incorporated into the cross-linked lattice. Hsu et al. use PVP/PVA as one type of "biocompatible agent." The critical aspect of Hsu et al. is that the coating is "stable." See the abstract of Hsu et al. In short, the coating described by Hsu et al. is the antithesis of a drug-eluting coating. A drug-eluting coating is necessarily an unstable coating because it is purposefully designed to release a drug entrained within it. In contrast, Hsu's coating is purposefully stable, including a cross-linked base layer that covalently bonds or physically entraps a hydrophilic, biocompatible agent, such as a PVP/PVA copolymer.

Note that Hsu et al. are totally silent with respect to the drug-elution qualities of their coating. That's because the Hsu et al. coating **is not** a drug-eluting coating at all. It is, by Hsu's own definition, a "stable" coating. See, for example, the paragraph starting at column 3, line 5 of Hsu et al., and the paragraph starting at column 4, line 53. The lubricity of Hsu et al.'s coating is entirely dependent upon the biocompatible agent, *i.e.*, the PVP/PVA copolymer being covalently linked to the cross-linked base layer or "stably" entrapped within the base layer. So if the base layer described by Ding, a non-cross-linked, ternary PVB copolymer, were used in place of the cross-linked based layer described by Hsu et al. (basically an epoxy glue), Hsu's device would fail because Hsu's PVP/PVA cannot be entrapped within the non-cross-linked PVB. Thus, the combination suggested by the Office would destroy the lubricity of Hsu et al.'s coating. The PVP/PVA coating would simply be washed away. (PVP/PVA is water-soluble; see the cover of the Kollidon reference.) The lubricity of the Hsu et al. coating is its intended utility. See Hsu et al. at column 5, lines 40-45. Therefore using Ding's PVB copolymer in combination with Hsu's PVP/PVA copolymer destroys the intended utility of the Hsu et al. coating because the PVP/PVA

must stay in place to achieve enhanced lubricity. It is well-settled law that when a proposed modification destroys the intended utility of one of the applied references, a *prima facie* case of obviousness has not been shown. See MPEP §2143.01(V) and the cases cited therein.

The Kollidon reference does not cure the shortcomings of the combination of Ding and Hsu et al. because (1) the utility of the coating described in Hsu et al. is still destroyed by the proposed combination; and (2) the Kollidon reference is devoted entirely to wet granulation and tabletting formulations. See Kollidon at section 3.2: "Kollidon... is an excellent binder for tablets and granules." See also Section 3.3 of the Kollidon reference: "The formulations in Tables 5 and 6 are typical formulations for tablet coatings." These coatings are meant for digestible tablets - tablets that will be exposed to the extremely acidic conditions of the stomach. These formulations having nothing whatsoever to do with implantable medical devices.

Note also that there is no motivation provided by any of Ding, Hsu et al. or the Kollidon reference to use PVP/PVA in Ding's formulation. As noted above, the combination destroys the utility of the Hsu et al. coating, so Hsu et al. actually teaches away from the combination. Ding is totally silent with respect to any PVP-containing polymer or copolymer, so it cannot provide any source of motivation for making the combination. And the Kollidon reference is directed to coatings for tablets, not implantable medical devices. Thus, the only source of motivation for making the combination is Applicants' own specification. However, the Office is not at liberty to use the Applicants' specification to provide the motivation or suggestion to combine that is absent from the applied references.

Lastly, note that the combined references do not even remotely suggest that a selectively tunable drug release coating can be obtained by combining PVB and PVP/PVA. On this point, see, for example, the passage at page 5 of the present application, the paragraph beginning at line 20, and continuing on to page 6:

> A further advantage of the inventive composition is that it allows greater control and selectivity of the drug release than prior art compositions. For example, many prior art compositions release the drug too quickly for it to have the required effect, and therefore drug release is controlled by the use of polymer-only top coatings or variations in the polymer:drug ratio of the coating.
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> The present composition is far more effective at providing a system with distinct and selective release profiles.

For these reasons, Applicants submit that the rejection of Claims 1-9 under 35 USC §103(a) over Ding, Hsu et al., and the Kollidon reference is improper. Withdrawal of the reference is respectfully requested.

Rejection of Claims 1-8 under 35 USC §103(a) Over Ding, in View of Hsu et al. and the Kollidon Reference, and Further in View of Sass (U.S. Patent No. 6,383,215):

Applicants respectfully traverse this rejection largely on the grounds articulated in the previous section of this response. Specifically, the combination of Ding, Hsu et al, and the Kollidon reference does not describe or suggest the three-part composition recited in Claim 1 because the references do not provide any motivation for combining a poly(vinyl butyral-co-vinyl alcohol-co-vinyl acetate) copolymer ("PVB," *i.e.*, the first compound) with a poly(vinyl pyrrolidone-co-vinyl acetate) copolymer ("PVP/PVA," *i.e.*, the second compound).

This rejection is also improper because combining Ding with Hsu et al. destroys the intended utility (drug elution) of the Ding device. Thus, the Office has not established a *prima facie* case of obviousness.

Applicants further traverse this rejection because the references themselves do not provide any motivation to make the combination. Applicants therefore submit that this rejection is improper because the Office is using Applicants' own specification to provide the motivation or suggestion that is lacking in the cited references.

The Ding patent describes using a PVB copolymer as a coating for an implantable medical device, including a stent. See Ding at column 2, lines 40-65. The Ding patent, however, is **completely silent** with respect to using any type of vinyl pyrrolidone-containing polymer or copolymer in combination with the PVB shown in Formula I of Ding (at the bottom of column 2). For example, Ding notes that "other examples" of polymers that can be used in his invention are poly(vinyl formal), poly(vinyl formal-co-vinyl alcohol-co-vinyl acetate, and mixed poly(acetal)-based polymers. These various copolymers can be used singly or blended. See Ding at column 2, lines 55-67. Nevertheless, Ding et al. neither describes, nor suggests using any type of vinyl pyrrolidone-containing polymer or copolymer.

The Office thus cites to the Hsu et al. patent for its description of a PVP/PVA copolymer. However, there is no motivation to combine Hsu et al. with Ding et al. because the manner in

which Hsu et al. use a PVP/PVA copolymer has nothing whatsoever to do with drug eluting devices. In fact, combining the PVP/PVA copolymer described by Hsu et al. with the PVB described by Ding destroys the intended utility of the Hsu et al. device. Applicants therefore submit that this rejection is improper.

Specifically, the abstract of the Hsu et al. patent states that biocompatible surfaces on medical devices are formed by creating a stable, lubricious, cross-linked base layer. Note, however, that this cross-linked base layer functions as an entrapping site for "biocompatible agents," which are then "stably" incorporated into the cross-linked lattice. Hsu et al. use PVP/PVA as one type of "biocompatible agent." The critical aspect of Hsu et al. is that the coating is "stable." See the abstract of Hsu et al. In short, the coating described by Hsu et al. is the antithesis of a drug-eluting coating. A drug-eluting coating is necessarily an unstable coating because it is purposefully designed to release a drug entrained within it. In contrast, Hsu's coating is purposefully stable, including a cross-linked base layer that covalently bonds or physically entraps a hydrophilic, biocompatible agent, such as a PVP/PVA copolymer.

Note that Hsu et al. are totally silent with respect to the drug-elution qualities of their coating. That's because the Hsu et al. coating **is not** a drug-eluting coating at all. It is, by Hsu's own definition, a "stable" coating. See, for example, the paragraph starting at column 3, line 5 of Hsu et al., and the paragraph starting at column 4, line 53. The lubricity of Hsu et al.'s coating is entirely dependent upon the biocompatible agent, *i.e.*, the PVP/PVA copolymer being covalently linked to the cross-linked base layer or "stably" entrapped within the base layer. So if the base layer described by Ding, a non-cross-linked, ternary PVB copolymer, were used in place of the cross-linked based layer described by Hsu et al. (basically an epoxy glue), Hsu's device would fail because Hsu's PVP/PVA cannot be entrapped within the non-cross-linked PVB. Thus, the combination suggested by the Office would destroy the lubricity of Hsu et al.'s coating. The PVP/PVA coating would simply be washed away. (PVP/PVA is water-soluble; see the cover of the Kollidon reference.) The lubricity of the Hsu et al. coating is its intended utility. See Hsu et al. at column 5, lines 40-45. Therefore using Ding's PVB copolymer in combination with Hsu's PVP/PVA copolymer destroys the intended utility of the Hsu et al. coating because the PVP/PVA must stay in place to achieve enhanced lubricity. It is well-settled law that when a proposed

modification destroys the intended utility of one of the applied references, a *prima facie* case of obviousness has not been shown. See MPEP §2143.01(V) and the cases cited therein.

The Kollidon reference does not cure the shortcomings of the combination of Ding and Hsu et al. because (1) the utility of the coating described in Hsu et al. is still destroyed by the proposed combination; and (2) the Kollidon reference is devoted entirely to wet granulation and tabletting formulations. See Kollidon at section 3.2: "Kollidon... is an excellent binder for tablets and granules." See also Section 3.3 of the Kollidon reference: "The formulations in Tables 5 and 6 are typical formulations for tablet coatings." These coatings are meant for digestible tablets - tablets that will be exposed to the extremely acidic conditions of the stomach. These formulations having nothing whatsoever to do with implantable medical devices.

The Sass patent is cited solely for its teaching of 17β-estradiol. 17β-estradiol is recited only in Claim 8 of the present application. Thus, the Sass patent is irrelevant to Claims 1-7 of the application.

Moreover, the only coating described in the Sass patent is diamond-like carbon (DLC). See Sass at column 3, lines 50-58. Therefore the coating described in Sass is unrelated to any of the coatings described by Ding, Hsu et al, and the Kollidon reference. In short, the underlying coating as recited in present Claim 1 is not taught or suggested by the combination of Ding, Hsu et al, and the Kollidon reference. Tossing Sass into the mix does not yield the present invention because there's no motivation to combine Ding, Hsu et al, and the Kollidon reference in the first place.

As noted earlier there is no motivation provided by any of Ding, Hsu et al. or the Kollidon reference to use PVP/PVA in Ding's formulation. The combination destroys the utility of the Hsu et al. coating, so Hsu et al. actually teaches away from the combination. Ding is totally silent with respect to any PVP-containing polymer or copolymer, so it cannot provide any source of motivation for making the combination. The Kollidon reference is directed to coatings for tablets, not implantable medical devices. And the only coating mention by Sass, diamond-like carbon, it totally unrelated to any copolymeric, drug-eluting coating. Thus, the only source of motivation for making the combination is Applicants' own specification. However, the Office is not at liberty to use the Applicants' specification to provide the motivation or suggestion to combine that is absent from the applied references.

Lastly, note that the combined references do not even remotely suggest that a selectively tunable drug release coating can be obtained by combining PVB and PVP/PVA. On this point, see, for example, the passage at page 5 of the present application, the paragraph beginning at line 20, and continuing on to page 6:

> A further advantage of the inventive composition is that it allows greater control and selectivtity of the drug release than prior art compositions. For example, many prior art compositions release the drug too quickly for it to have the required effect, and therefore drug release is controlled by the use of polymer-only top coatings or variations in the polymer:drug ratio of the coating.
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> The present composition is far more effective at providing a system with distinct and selective release profiles.

For these reasons, Applicants submit that the rejection of Claims 1-8 under 35 USC §103(a) over Ding, Hsu et al., the Kollidon reference, and Sass et al. is improper. Withdrawal of the reference is respectfully requested.

Respectfully submitted,

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